

A listing of claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

1-27. (Canceled)

28. (Previously presented) A method of designing amino acid sequences of variable domains of a humanized monoclonal antibody comprising:

(a) comparing the amino acid sequences of the light and heavy chain variable domains of a monoclonal antibody to be humanized with the amino acid sequences of the light and heavy chain variable domains of two or more human antibodies;

(b) selecting framework regions from a first human antibody for the light chain and from second and third human antibodies for the heavy chain based on the sequence comparison, wherein the heavy chain FR1, FR2 and FR3 are selected from the second human antibody and FR4 is selected from the third human antibody; and

(c) incorporating the framework regions selected in step (b) with the corresponding light and heavy chain complementarity determining regions of the monoclonal antibody to be humanized, to design humanized light and heavy chain variable domain amino acid sequences

wherein the heavy chain FR4 is selected from the human NEWM antibody, the light chain framework regions are selected from the human REI antibody, and the heavy chain FR1, FR2 and FR3 are selected from the human EU antibody.

29. (Previously presented) The method according to claim 28, further comprising retaining selected amino acid residues from the framework regions of the monoclonal antibody to be humanized in the corresponding framework regions of the humanized variable domains where said selected amino acids are predicted to have contacts with said complementarity determining regions.

30. Canceled.

31. (Previously presented) The method according to claim 29, wherein said selected amino acid residues are within a 4.5 Angstrom radius of any atoms within a complementarity determining regions of the light or heavy chain of the humanized monoclonal antibody.

32. (Previously presented) The method of claim 28, further comprising:

(d) preparing a DNA sequences encoding the humanized light and heavy chain variable domain amino acid sequences;

(e) operably incorporating the variable domain DNA sequences into at least one vector comprising DNA sequences encoding the constant domains of the human light and heavy chain regions;

(f) introducing the at least one vector into a cell; and

(g) culturing the cell containing the at least one vector under conditions to produce the humanized monoclonal antibody.

33-43. (Canceled)

44. (Currently amended) A method of designing amino acid sequences of variable domains of a humanized monoclonal antibody comprising:

(a) comparing the amino acid sequences of the light and heavy chain variable domains of a monoclonal antibody to be humanized with the amino acid sequences of the light and heavy chain variable domains of two or more human antibodies;

(b) selecting framework regions from a first human antibody for the light chain and from second and third human antibodies for the heavy chain based on the sequence comparison, wherein the heavy chain FR1, FR2 and FR3 are selected from the second human antibody and FR4 is selected from ~~the~~ a single third human antibody; and

(c) incorporating the framework regions selected in step (b) with the corresponding light and heavy chain complementarity determining regions of the monoclonal antibody to be humanized, to design a humanized light and heavy chain variable domain amino acid sequences.

45. (Previously presented) The method according to claim 44, further comprising retaining selected amino acid residues from the framework regions of the monoclonal antibody to be humanized in the corresponding framework regions of the humanized variable domains where said selected amino acids are predicted to have contacts with said complementarity determining regions.

46. (Previously presented) The method according to claim 45, wherein said selected amino acid residues are within a 4.5 Angstrom radius of any atoms within a complementarity determining regions of the light or heavy chain of the humanized monoclonal antibody.

47. (Previously presented) The method of claim 44, further comprising:

(d) preparing a DNA sequences encoding the humanized light and heavy chain variable domain amino acid sequences;

(e) operably incorporating the variable domain DNA sequences into at least one vector comprising DNA sequences encoding the constant domains of the human light and heavy chain regions;

(f) introducing the at least one vector into a cell; and

(g) culturing the cell containing the at least one vector under conditions to produce the humanized monoclonal antibody.